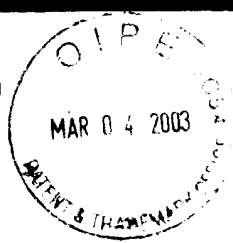


In re Application of:
Worley and Brakeman
Application No.: 09/910,706
Filed: July 20, 2001
Listing of Claims - Page 1



PATENT
Attorney Docket No.: JHU1520-2

LISTING OF CLAIMS

Claim 1. (Original) An isolated polynucleotide capable of encoding a polypeptide having substantial sequence identity to the sequence SEQ ID NO: 2 and characterized by (i) enhanced expression in mammalian central nervous tissue in response to synaptic activation, and (ii) a PDZ-like domain coding region.

Claim 2. (Original) The isolated polynucleotide of claim 1, wherein said sequence identity is at least about 80%.

Claim 3. (Original) The isolated polynucleotide of claim 1, wherein said polynucleotide has the sequence SEQ ID NO: 1.

Claim 4. (Original) An isolated polypeptide, characterized by (i) enriched expression during synaptic activity in mammalian brain, (ii) presence of a PDZ-like binding domain, and (iii) a sequence that is at least 80% identical to SEQ ID NO: 2.

Claim 5. (Original) The isolated polypeptide of claim 4, which further exhibits an ability to selectively bind to a synaptic membrane protein having a C-terminal peptide region selected from the group consisting of SSSL and SSTL.

Claim 6. (Original) The isolated polypeptide of claim 4, wherein said sequence identity is at least about 80%.

Claim 7. (Original) The isolated polypeptide of claim 6, wherein said polypeptide has the sequence SEQ ID NO: 2.

Claim 8. (Original) A vector which contains a polynucleotide capable of encoding a polypeptide having at least about 80% sequence identity to the sequence SEQ ID NO: 2 and characterized by enhanced expression in central nervous tissue in response to synaptic activation.

Claim 9. (Original) The vector of claim 8, wherein said polynucleotide has the sequence SEQ ID NO: 1.

Claim 10. (Currently Amended) A method of selecting a compound that interferes with [biding] binding of a synaptic activation protein to a cellular binding protein in the mammalian central nervous system, comprising:

adding a test compound to a reaction mixture containing (i) [an isolated] a synaptic activation protein having [substantial] at least 70% sequence identity to a polypeptide having the sequence SEQ ID NO:2, (ii) [an isolated] a binding protein to which [said] the synaptic activation protein binds, and (iii) means for detecting binding between [said] the synaptic activation protein and [said] the binding protein; measuring binding between [said] the synaptic activation protein and [said] the binding protein; and

selecting [said] the compound if the measured binding is greater than or less than binding measured in the absence of [said] the test compound.

Claim 11. (Currently Amended) The method of claim 10, wherein [said] the binding protein is a metabotropic glutamate receptor (mGluR) [which includes a sequence selected from the group consisting of SSSL and SSTL].

Claim 12. (Currently Amended) The method of claim [11] 26, wherein [said] the binding protein comprises a mGluR [binding protein is expressed in cells,] and [said binding between said receptor] the measuring the cellular response to binding between the synaptic binding protein and [said] the binding protein [is measured by] comprises measuring phosphoinositidase C (PI-PLC) activity in [said] the cells.

Claim 13. (New) The method of claim 10, wherein the binding protein is a metabotropic glutamate receptor comprising a sequence selected from the group consisting of SSSL and SSTL.

Claim 14. (New) The method of claim 11, wherein the mGluR is selected from mGluR5 and mGluR1 α .

Claim 15. (New) The method of claim 10, wherein the synaptic activation protein is a Homer protein.

Claim 16. (New) The method of claim 10, wherein the synaptic activation protein is in solid phase.

Claim 17. (New) The method of claim 16, wherein the solid phase is a microtiter plate.

Claim 18. (New) The method of claim 10, wherein the means for detecting binding is a glutathione-S-transferase (GST)-pulldown.

Claim 19. (New) The method of claim 10, wherein the means for detecting binding is coimmunoprecipitation.

Claim 20. (New) The method of claim 10, wherein the measuring binding comprises labeling the binding protein, wherein the labeling is direct labeling or is subsequent addition of a labeled, binding protein-specific reagent.

Claim 21. (New) The method of claim 20, wherein the binding protein-specific reagent is an antibody.

Claim 22. (New) The method of claim 20, wherein the labeling comprises use of an enzyme capable of generating a signal, use of a radiolabeled reagent, use of a fluorescent dye, or use of gold or biotin.

Claim 23. (New) The method of claim 22, wherein the radiolabeled reagent is labeled with ¹²⁵I.

Claim 24. (New) A pharmaceutical composition containing a compound identified by the method of claim 10.

Claim 25. (New) A method of treating a condition comprising administration of an effective amount of a compound identified by the method of claim 10, wherein the condition is characterized by an altered neuronal and/or synaptic activity.

Claim 26. (New) The method of claim 25, wherein the condition comprises epilepsy, abnormal brain development, neural injury, trauma or chemical addiction.

Claim 27. (New) A method of identifying a compound that modulates a cellular response, comprising:

adding a test compound to a cell containing: (i) a synaptic activation protein having at least 70% sequence identity to a polypeptide having the sequence SEQ ID NO:2, (ii) a binding protein to which the synaptic activation protein binds, and (iii) means for detecting cellular response to binding between the synaptic activation protein and the binding protein;

measuring the cellular response to binding between the synaptic activation protein and the binding protein; and

comparing the cellular response in the presence and absence of the test compound, wherein a change in the cellular expression in the presence of the compound as compared to the absence of the compound is indicative of a compound that modulates a cellular response.

Claim 28. (New) The method of claim 27, wherein the cell comprises a bacterial, yeast, insect or mammalian cell.

Claim 29. (New) The method of claim 27, wherein the synaptic activation protein is expressed by a gene endogenous to the cell.

Claim 30. (New) The method of claim 27, wherein the synaptic activation protein is expressed by a gene construct transfected into the cell.

Claim 31. (New) The method of claim 27, wherein the binding protein is expressed by a gene endogenous to the cell.

Claim 32. (New) The method of claim 27, wherein the binding protein is expressed by a gene construct transfected into the cell.

Claim 33. (New) The method of claim 27, wherein the measuring the cellular response to binding between the proteins comprises a two-hybrid protein interaction assay.

Claim 34. (New) The method of claim 27, wherein the measuring the cellular response to binding between the proteins comprises using a reporter construct.

Claim 35. (New) The method of claim 34, wherein the reporter construct comprises a vector comprising a polynucleotide encoding an isolated synaptic activation protein having at least 70% sequence identity to a polypeptide having the sequence SEQ ID NO:2.

Claim 36. (New) The method of claim 35, wherein the reporter construct further comprises at least one regulatory sequence.

Claim 37. (New) The method of claim 27, wherein the measuring the cellular response to binding between the proteins comprises using a mGluR construct comprising a binding protein, wherein the binding protein comprises mGluR.

Claim 38. (New) The method of claim 37, wherein the mGluR comprises a sequence selected from the group consisting of SSSL and SSTL.

Claim 39. (New) The method of claim 37, wherein the mGluR is selected from mGluR5 and mGluR1 α .

Claim 40. (New) The method of claim 27, wherein the cellular response comprises an increase or decrease in calcium mobilization or PI-PLC activity.

Claim 41. (New) A pharmaceutical composition containing a compound identified by the method of claim 27.

Claim 42. (New) A method of treating a condition comprising administration of an effective amount of a compound identified by the method of claim 27, wherein the condition is characterized by an altered neuronal and/or synaptic activity.

Claim 43. (New) The method of claim 42, wherein the condition comprises epilepsy, abnormal brain development, neural injury, trauma or chemical addiction.